REMARKS

I. Status of the Claims

Claims 8-24, 26-29 and 39-41 are currently pending in this application and stand rejected. Claims 1-7, 25, and 30-38 have been cancelled. Claims 8, 11, 12, 17, and 19 are currently amended.

Support for the amendments to claims 8, 11, 12, 17, and 19 can be found, for example, at page 9, lines 17-20 of the specification. Specifically, each of these claims has been amended to recite formula (I) compounds where R^4 together with $-OR^{28}$ forms a lactone. Exemplary compounds exhibiting this structural feature include Gibberellins A_3, A_4, and A_7. *See, e.g., Specification* at 23.

Accordingly, Applicants submit that no new matter has been added by these amendments.

II. Interview Summary

Applicants appreciate the courtesy of an after final interview with the Examiner on May 4, 2007, the proceedings of which are reflected in part by the Interview Summary dated May 8, 2007. In discussing the pending rejections, Applicants urged that the disclosure of three representative Gibberellin species in the specification fully enables the claimed genus based on the generally-predictable efficacy of the Gibberellin class of compounds as a whole. In addition, Applicants submitted that the specification in combination with the knowledge of one of ordinary skill in the art would enable the skilled artisan to synthesize and/or isolate and determine the efficacy of the claimed Gibberellin compounds of formula (I) by routine experimentation.

Applicants appreciate the Examiner's general acknowledgement of the substance and merit of the Applicants' arguments during the interview. However, the Examiner did not agree with Applicants' argument that the specification statements regarding the overall efficacy of the Gibberellin class of compounds coupled with the disclosed exemplary species sufficiently enabled the claimed genus. The Examiner did encourage the Applicants to submit extrinsic evidence supporting the general efficacy of the claimed Gibberellin genus as a whole. In addition, the Examiner acknowledged that amending the pending claims to further focus the scope of the claimed genus may place them in condition for allowance.

Should the Examiner disagree with the Applicants' presentation of the substance of the interview, or if Applicants have misunderstood any of the Examiner's positions, Applicants respectfully request the Examiner to clarify in writing.

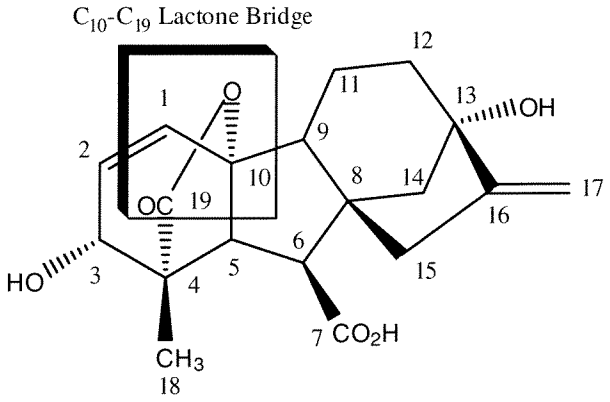
III. Rejections Under 35 U.S.C. § 112, ¶ 1

The Examiner has rejected claims 8, 11-24, 26-29 and 39-41 under 35 U.S.C. § 112, ¶ 1, as allegedly failing to comply with the enablement requirement. *Final Office Action* at 2. Applicants respectfully traverse this rejection.

The Examiner alleges that the specification does not enable "the treatment of diabetes with Gibberellins of Formula (1)." *Id.* at 2. The Examiner admits that the specification enables the treatment of diabetes with Gibberellin A3 and a mixture of Gibberellin A3 and A4/A7, but alleges that the treatment of diabetes with Gibberellins of formula (1) is not enabled due to the number of species encompassed by the claimed genus. *Id.* at p. 3.

Specifically, the Examiner contends that the disclosure of Gibberellins A3, A4, and A7 "is not commensurate with the full scope of the claimed invention" because the "present claims encompass an immense number of species." *Id.* at 4. According to the Examiner, the claims "encompass compounds having major variations in structural formulas," while the three exemplary Gibberellin species exhibit "closely related structural formulas." *Id.* Applicants respectfully disagree for the reasons already of record and in view of the present amendments to the pending claims.

Initially, Applicants note that claims 8, 11, 12, 17, and 19 have been amended to focus the claimed genus on Gibberellin species comprising a C_{10}-C_{19} lactone bridge:



Gibberellin A_3

The amended claims encompass the structural characteristics of the three Gibberellin species disclosed in the specification, and significantly reduce the number of Gibberellin species covered. For example, in 2002, *Mander* disclosed the structures of approximately 130 naturally-occurring Gibberellin species known at that time. *See Nat. Prod. Rep.*, 20:49-69, 50-51 (2003) ("Mander"). Applicants estimate that prior to this amendment, the claimed formula (I) genus would have encompassed at least 80% of the compounds disclosed in *Mander*. However, Applicants believe that the present

claim amendments have focused the claim scope to less than 60% of *Mander's* disclosed compounds.

As previously argued, "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent *coupled with information known in the art* without undue experimentation." M.P.E.P. § 2164.01 (emphasis added); *see also In re Wands,* 858 F.2d 731, 737 (Fed. Cir. 1988). Moreover, the Federal Circuit has stated that Applicants "are not required to disclose each and every species encompassed by their claims even in an unpredictable art." *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976). The Court has also noted that a genus may be enabled "by showing the enablement of a *representative number* of species within the genus." *Regents of Univ. of Cal. v. Eli Lilly & Co.,* 119 F.3d 1559 , 1569 (Fed. Cir. 1997) (emphasis added). "For a claimed genus, representative examples together with a *statement applicable to the genus as a whole* will ordinarily be sufficient if one skilled in the art ...would expect the claimed genus could be used in that manner without undue experimentation." M.P.E.P. §2164.02 (emphasis added); *see also In re Grimme,* 274 F.2d 949 (C.C.P.A. 1960).

The question as to the sufficiency of a disclosure to support a generic claim has been frequently considered by the Court. For example, in *In re Grimme*, 274 F.2d 949, cited in *Lilly,* 119 F.3d at 1569, which related to a substituted penicillin, the Court considered whether the substituent group had adequate support in the parent and stated:

> [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, it may not be necessary

> to enumerate a plurality of species if a genus is sufficiently identified in an application by "other appropriate language."
>
> What constitutes "other appropriate language" within the meaning of the cited cases will, of course, depend on the circumstances of the particular case.

Id. at 952 (citations omitted).

In view of the present amendments, Applicants note a total of three species disclosed in the specification that are representative of the claimed formula (I) genus as amended. In addition to the three representative examples of the claimed Gibberellin species, the specification contains several "general statements applicable to the genus as a whole." *See* M.P.E.P. §2164.02. For example, such Gibberellins in general "possess growth factor (such as IGF, EGF) like properties" that act "on a broader (less specific) base than that of the more complex life forms such as animals." *Specification* at 4. Additionally, "compounds of formula (1) possess activity as insulin and insulin like agonists and/or sensitizers for the treatment of diabetes, its complications and associated conditions..." *Id.* at 12. The specification further indicates that Gibberellins may act as substitutes or sensitizers for growth factors, including IGF-1, which elicit effects similar to insulin. *Id.* at 5.

Moreover, the generally consistent efficacy of Gibberellins comprising a C_{10}-C_{19} lactone bridge is well documented. *Reeve et al.* recognized the association between biological activity and the compatibility between Gibberellins and receptors in plant systems. For example, in the barley aleurone bioassay, a high degree of biological activity is associated with Gibberellins having a γ-lactone residue (C_{10}-C_{19} lactone bridge). *J. Exper. Bot.,* 85:431-445, 431 (1974) ("Reeve"); *see also Plant Cell Physiol.,* 36:1205-1211 (1995) (finding that Gibberellins A1, A4, A9 and A20 (all comprising a

C_{10}-C_{19} lactone bridge) are effective in promoting germination). Similarly, only Gibberellins having a γ-lactone or a δ-lactone (C_{10}-C_{20} lactone bridge) group resulted in substantial activity in the cucumber bioassay. *Id.*

U.S. Patent No. 5,580,857 to Oden exemplified the efficacy of Gibberrellins comprising a C_{10}-C_{19} lactone bridge in mammalian systems. Oden demonstrated that Gibberellins A7 and A20/A30 are useful in the treatment of psoriasis and prostatitis, respectively. *Oden* at col. 13, ll. 10-65 and col. 14, ll. 7-17. In particular, Oden recognized that "[t]he most effective gibberellins for the treatment of hypertrophy and hyperplastic adenoma in the prostate are lactonic C-19 gibberellins hydroxylated in position 12." Other therapeutically-active compounds include lactonic C_{19} gibberellins with no hydroxyl group and lactonic C_{19} gibberellins hydroxylated at positions 3 or 13. *Id.* at col. 7, ll. 39-51. Applicants note that Gibberellins A3, A4, and A7 comprise a larger group of especially preferred compounds of the invention. *Id.* at col. 4, ll. 23-26 and col. 7, ll. 47-49.

Oden has also recognized the general efficacy of Gibberellin conjugates. *Id.* at col. 8, ll. 55-6 ("[t]he activity of gibberellin conjugates depends on the hydrolysis to free gibberellins"). Preferred conjugates disclosed in Oden include glycosylic ethers and esters. *Id.* at col. 4, ll. 63-65 and col. 5, ll. 10-12. According to Oden, the activity of Gibberellin conjugates in mammalian systems can be traced to the "enzymatic cleavage by e.g. glucosidase or by extreme pH values." *Id.* at col. 8, ll. 6-10. This teaching suggests that a wide variety of Gibberellin derivatives may be synthesized and administered to mammals to yield biologically-active Gibberellins *in vivo.*

In summary, the combined teachings of Reeve and Oden suggest that Gibberellins comprising a C_{10}-C_{19} lactone bridge exhibit enhanced biological activity in both plant and animal systems, respectively. Oden also supports the proposition that minor variations to the substitutents comprising the C_{10}-C_{19} Gibberellin backbone may be tolerated in mammalian systems without sacrificing therapeutic activity. In addition, Oden teaches that Gibberellin derivatives, comprising substituents such as glycosylic ether and esters, yield the therapeutically-active Gibberellin via enzymatic hydrolysis.

Teachings from the specification of the present application, in conjunction with the exemplary Gibberellins disclosed therein, parallel the conclusions reached in Reeve and Oden. Examples 3 and 4 of the present application (*Specification* at 20-21) demonstrate that minor variations in structure have little or no effect on the *growth factor-mimicking* activity of Gibberellins in mammalian cells. Examples 5 and 6 (*Id.* at 21-23) demonstrate that such variations elicit little or no effect on the *in vivo anti-diabetic* activity of Gibberellins. Moreover, the specification provides a method by which the skilled artisan can synthesize Gibberellin derivatives and test the efficacy of the compounds encompassed by the claims. *See id.* at 2-3 and 22-23. Therefore, based on the exemplary Gibberellins and the known teachings concerning the generally consistent efficacy of the Gibberellins encompassed by the pending claims, Applicants respectfully submit that the specification fully enables a person of ordinary skill in the art to practice the invention without undue experimentation.

Accordingly, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112.

IV. Objection to Claims 9 and 10

The Examiner has objected to claims 9 and 10 for being dependent upon rejected base claim 8. *Final Office Action* at 4. However, the Examiner has stated that the claims "would be allowable if rewritten in independent form including all of the limitations of the base claim." *Id.*

In view of the presently amended claims and arguments submitted therewith, Applicants respectfully submit that this objection will be rendered moot upon allowance of claim 8 and request the Examiner reconsider this objection accordingly.

Accordingly, Applicants respectfully request withdrawal of this objection.

V. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. If the Examiner has any questions, regarding this Amendment and Response, the Examiner is invited to contact the undersigned at 617-452-1608.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: June 29, 2007

By: _____
Mike McGurk
Reg. No. 32,045